

Bronchiolitis Obliterans Organising Pneumonia: A Treatable Condition

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Summary

Bronchiolitis obliterans organising pneumonia (BOOP) is an uncommon inflammatory lung condition involving the terminal bronchioles and alveoli, which is responsive to treatment with corticosteroids. Patients usually present with dyspnoea, cough and fever. Two cases are described here: both had haemoptysis and were initially treated as community acquired pneumonia. Diagnosis was made on lung biopsy and there was rapid resolution after a course of prednisolone.

Key Words: Bronchiolitis obliterans organising pneumonia, Corticosteroids

Introduction

Bronchiolitis obliterans organising pneumonia was described in 1985 as a distinct clinicopathologic syndrome characterised by a "pneumonia-like" illness with proliferation of granulation tissue within small airways and alveolar ducts associated with chronic inflammation in the surrounding alveoli¹. A new classification of the idiopathic interstitial pneumonias developed by an international panel has suggested the name "cryptogenic organizing pneumonia"². It has been reported throughout the world. Most patients have idiopathic BOOP although it has several known causes and associated systemic disorders including respiratory infections, drugs and toxins, connective tissue diseases, radiotherapy and immunological disorders³. Therefore, the condition can be considered to be a non-specific excessive response to many types of lung injury. In BOOP, lung architecture is preserved and the newly formed fibromyxoid connective tissue plugging the bronchioles and alveoli can be reversed by corticosteroid therapy.

Case 1

A 43-year-old Chinese lady presented in October 1998 with a 3-week history of cough and intermittent fever.

Her sputum was mucoid and occasionally blood-stained. There was no past medical history apart from a thyroid operation 6 years previously and she had never smoked. She worked as an accounts clerk in an electronics factory. Her chest radiograph taken at another hospital showed consolidation in the right middle lobe with patchy alveolar opacities in the right upper zone and left base. She was given intravenous cefuroxime for 4 days and was started on a therapeutic trial of anti-tuberculosis drugs when the fever failed to settle. She underwent bronchoscopy which did not show any abnormality. However, cytological examination of bronchial brushings and washings revealed atypical cells and cells suspicious of a malignancy.

On examination, she looked well, had a transverse neck scar and did not have finger clubbing. There were crepitations in the right lower zone but no other abnormalities. Sputum culture was negative for bacterial pathogens and mycobacteria. Sputum smears were negative for acid fast bacilli and sputum cytology was negative for malignant cells. Mantoux test was positive at 15 mm. The following blood investigations were normal: full blood count, renal profile, liver

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function tests, blood glucose, arterial blood gases, coagulation screen, rheumatoid factor, antinuclear factor and anti-HIV antibody. Erythrocyte sedimentation rate (ESR) was 28 mm/hour. Repeat chest radiograph showed the bilateral opacities noted earlier and computed tomography (CT) scan of thorax showed multiple areas of ground glass opacities in both lungs with consolidation in the apical and posterior basal segments of the left lower lobe. Pulmonary function tests revealed a restrictive ventilatory defect, with reduced lung volumes and diffusing capacity for carbon monoxide.

She was readmitted and treated with intravenous cefoperazone and oral erythromycin for 2 weeks. Anti-tuberculosis drugs were stopped. Low-grade fever and production of blood-stained sputum persisted, and the opacities on the chest radiograph did not resolve. Repeat bronchoscopy showed inflammation of the right middle lobe. Bronchial biopsies, culture and cytology of bronchial washings showed no specific pathology. Video-assisted thoracoscopic biopsy of the right middle lobe under general anaesthesia was performed. Histopathological examination of the lung biopsy showed fibroblastic plugs obstructing bronchioles and some alveoli (Masson bodies) and interstitial infiltration with lymphocytes, plasma cells and macrophages, consistent with bronchiolitis obliterans organising pneumonia (Fig. 1). She was discharged on a course of prednisolone which was tailed off over several weeks. There was rapid resolution of both symptoms and radiological changes. She remained well up until she was last seen in October 2002.

Case 2

A 67-year-old Chinese man was seen in September 2003 with a 3-month history of cough and breathlessness. Soon after these symptoms started in June 2003, he was admitted to another hospital with acute onset of haemoptysis. He had a past history of diabetes mellitus for 10 years which was treated with gliclazide, metformin and rosiglitazone. He was an ex-smoker and worked part-time as a company manager. Chest radiograph on admission showed left upper zone opacity. CT scan of the thorax showed a lesion measuring 3 x 4 cm with irregular spiculated margins suggestive of a malignant lesion (Fig. 2). There were also incidental findings of cholelithiasis, a right thyroid nodule (2 x 3cm) and a left adrenal nodule (1cm). Full blood count showed normal haemoglobin with raised white cell count and polymorphonuclear leucocytosis. The following blood investigations were normal: renal

profile, liver function tests and serum thyroxine. Random blood glucose was 11.3 mmol/L and ESR was 66 mm/hour. CT scan guided percutaneous trucut lung biopsy was performed and histopathological findings were consistent with bronchiolitis obliterans organising pneumonia: there was thickening of the interalveolar septae and blood vessel walls with obliteration of the alveolar lumen in many places by granulation tissue containing mixed inflammatory cells, histiocytes and fibroblasts. His sputum grew *Klebsiella pneumoniae* and he was treated with 3 consecutive courses of oral antibiotics (cotrimoxazole, cefprozil and levofloxacin). His haemoptysis stopped but cough and breathlessness persisted.

When seen by the author in September 2003, he was well, normotensive and had no abnormal physical signs apart from a mobile 2 cm nodule in the right thyroid. Repeat chest radiograph showed persistent left upper lobe opacity. By this time, sputum culture was negative for bacterial pathogens and sputum smears for acid fast bacilli were negative. Full blood count, renal profile, liver function tests and serum calcitonin were normal. Random blood glucose was 11.2 mmol/L and ESR was 10 mm/hour. Spirometry showed normal ventilatory function. A course of prednisolone was started and tailed off over several weeks. There was rapid improvement of respiratory symptoms and radiological changes and he remained well until last seen in January 2004. He was referred to an endocrinologist for further management of the asymptomatic thyroid and adrenal nodules.

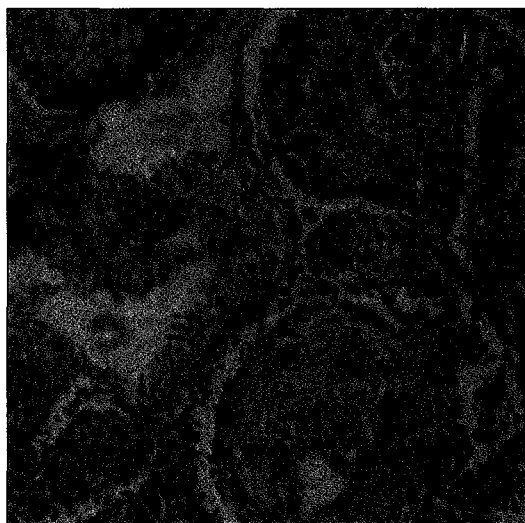


Fig. 1: Lung biopsy from Case 1, showing fibroblastic plug in bronchiole

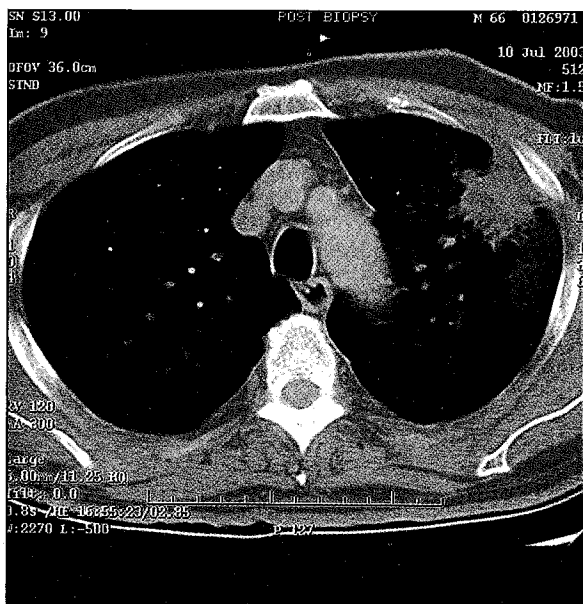


Fig. 2: CT scan thorax from Case 2, showing a focal lesion with irregular spiculated margins in the left upper lobe

Discussion

The typical patient with BOOP presents with dyspnoea, cough, fever, and a chest radiograph with bilateral multiple alveolar opacities. Such features may be mistaken for pneumonia. Men and women are affected equally, usually in the fifth and sixth decades. Haemoptysis, which was present in both the patients reported here, is not a common symptom although it has been reported as a presenting complaint⁴. Clubbing is rare, two thirds of patients have crackles on auscultation and pulmonary function tests most often show restrictive ventilatory defect with impaired diffusing capacity. The chest radiograph characteristically shows bilateral patchy infiltrates with no loss of lung volume. The chest CT scan usually shows bilateral areas of consolidation and ground glass opacities, mainly with peripheral location. Focal nodular BOOP can occur and may be clinically indistinguishable from carcinoma of the lung.

Lung biopsy is needed for establishing the diagnosis, which depends on both the clinical setting and finding


the characteristic pathologic features of the disease. Open lung biopsy has long been considered the gold standard for the diagnosis of parenchymal lung disease but the video-assisted thoracoscopic procedure has become the established technique². Transthoracic CT-guided biopsy (the method used for Case 2) is not a common mode of diagnosis but can be considered for peripheral lung lesions. It is also necessary to perform a thorough search to rule out the many possible causes of BOOP.

The prognosis for idiopathic BOOP is good and 65% to 80% of patients treated with corticosteroid therapy are cured. The mortality rate from the original series was 6%¹. The first-line treatment for patients with symptomatic and progressive disease is prednisolone. Clinical improvement is rapid, usually within several days or a few weeks and can be quite dramatic in some patients. There is usually complete radiological resolution or minimal residual scarring. The recommended duration of treatment is a year although a shorter 6-month course has been deemed sufficient in certain situations³. BOOP may recur in a third of patients treated for less than one year; these patients usually respond a second or third time to the previously responsive dose of corticosteroid. Anecdotally, other drugs have been used to treat this condition but epidemiological studies have not yet been done to confirm their efficacy. Spontaneous improvement appears to occur over 3 to 6 months in some patients¹.

In summary, 2 cases of histologically confirmed BOOP are described in whom haemoptysis was an important presenting symptom. BOOP should be considered in any patient with respiratory illness and unexplained radiographic infiltrates, not responsive to antibiotics. It is important to obtain histological diagnosis because this is a benign inflammatory lung disease with good prognosis which responds to corticosteroids

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